



## MONOCLONAL ANTIBODY FRAGMENTS FOR TARGETING THERAPEUTICS TO GROWTH PLATE CARTILAGE

### SUMMARY

The NICHD seeks statements of capability or interest from parties interested in collaborative research to co-develop, evaluate, or commercialize treatment of skeletal disorders using targeting antibodies.

### REFERENCE NUMBER

E-003-2014

### PRODUCT TYPE

- Therapeutics

### KEYWORDS

- growth plate
- human growth hormone
- skeletal dysplasia
- short stature

### COLLABORATION OPPORTUNITY

This invention is available for licensing and co-development.

### CONTACT

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### DESCRIPTION OF TECHNOLOGY

A child's growth is dependent on the proper functioning of the growth plate, a specialized cartilage structure located at the ends of long bones and within the vertebrae. Failure of the growth plate to function properly can result in short stature or sometimes a skeletal dysplasia, such as achondroplasia, in which the bones are not just short but also malformed. Current treatments for severe short stature and skeletal growth disorders are limited. Recombinant human growth hormone (GH) is typically used, but the results are often less than optimal and growth hormone has potential adverse effects.

Researchers at the NICHD [Section on Growth and Development](#), collaborating with the [NCI Laboratory of Experimental Immunology](#), created human monoclonal antibody fragments that bind to matrilin-3, a protein specifically expressed in cartilage tissue. When injected intravenously in mice, these antibody fragments homed to cartilage and were not detectable in other tissues. Coupling these cartilage-binding



antibodies to growth-stimulating endocrine factors, such as growth hormone and IGF-I, and paracrine factors, such as CNP, could allow therapy targeted specifically to growth plate, and also articular cartilage, thereby opening up broad new pharmacological approaches to treat skeletal dysplasias and short stature. The same approach could also be used in adults to treat articular cartilage diseases like osteoarthritis. The research is currently in preclinical development, with *in vitro* data and *in vivo* mouse model data demonstrating that these antibody fragments target cartilage *in vivo*.

The researchers are interested in a collaboration to explore applications of this new approach. For example, a collaborator could produce fusion proteins combining the antibody fragments with various chondrogenic proteins that enhance growth. The collaborator might produce and purify the fusion proteins, which could then be tested for therapeutic effects in mice by the NICHD investigators.

## POTENTIAL COMMERCIAL APPLICATIONS

A new treatment option for cartilage disorders, such as (1) skeletal dysplasias, (2) short stature, and (3) articular diseases like osteoarthritis.

## COMPETITIVE ADVANTAGES

Avoidance of the risks associated with systemic treatment using growth hormone, such as increased intracranial pressure, slipped capital femoral epiphysis, insulin resistance, and possibly type II diabetes.

## INVENTOR(S)

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## DEVELOPMENT STAGE

- Pre-clinical (in vivo)

## PUBLICATIONS

[Pharm Res. 2015 Jul;32\(7\):2439-49. doi: 10.1007/s11095-015-1636-z. Epub 2015 Feb 19.](#)

## PATENT STATUS

- **U.S. Filed:** US Application No. 61/927,904 filed 15 Jan 2014

## THERAPEUTIC AREA

- Musculoskeletal